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(v) determining whether said amplified target and reference sequences are hybridized with said probes homologous therewith, false negative data being indicated by failure of said probes to hybridize either to the sample or to the reference sequence and false positive data being indicated by hybridization of the target sequence probe and by the absence of hybridization of the reference sequence probe.--

REMARKS

The Invention

The invention defined by pending claims 18-25 and 31-33 is a method for discerning the presence of false positive data or false negative data in an assay for the detection of a target viral RNA sequence.

This invention is defined by original claim 18, as rewritten, and as set forth in the foregoing amendment to the specification which paraphrases claim 18.

An important aspect of the invention includes quantification of the target viral sequence through the use of labelled probes. See claims 31-33.

The manner in which false positive or false negative data is discerned by the claim 18 process is apparent from the following table.

Result	Target	Reference Sequence	
1	+	+	Positive
2	0	+	Negative1/
3	0	0	False Negative2/
4	+	0	False Positive

1/ Correct function of the assay is evidenced by probe hybridzation only to the reference sequence.

2/ The reference probe would have hybridized if the assay were functioning correctly. It did not, hence the negative result for the target is false.

Original claim 18, as amended, and claims 31-33 conform to the specification of this application as filed. See, e.g., page 2, lines 11-15, page 4, lines 1-22, and page 7, line 1 to page 8, line 4. See also Example V, page 11, et. seq., Example VI and Example VII, page 12. See also original claims 18-30.

The Rejection of Claim 18 "Under 35 U.S.C. §102(b) As Being Clearly Anticipated by Mullis et al." (Paper No. 9, pp. 4-5)

Reference to the foregoing table shows that the rejection of claim 18, either as originally presented or as rewritten, is incorrect. Claim 18 requires the addition of a reference sequence (see step (ii)(b)) to the target viral sequence. The target viral sequence and the reference sequence are simultaneously amplified and otherwise processed in the manner defined by steps (iii), (iv) and (v) of the claim.

No such reference sequence is understood to be disclosed or suggested by Mullis, et al. In particular, the portions of that reference cited in Paper No. 9 do not appear to include and are not urged by the Examiner to include the disclosure or suggestion of such a reference sequence in the amplified procedure.

The Federal Circuit has repeatedly stated that anticipation is established only when each and every element of the claimed invention is disclosed either expressly or under the principles of inherency in a single prior art reference. See, e.g., Kalman v. Kimberly-Clark Corp., 713 F.2d 760, 771, 218 USPQ 781, 789 (Fed. Cir. 1983), cert. denied, 465 U.S. 1026 (1984).

The Mullis references does not satisfy that standard.

Withdrawal of the rejection of claim 18 as anticipated by Mullis is requested.

The §103 Rejections Based on Mullis
In View of Ratner, Hennighausen and Wathen

In each case the primary reference, Mullis, fails for the reasons set forth with respect to the rejection based on 35 U.S.C. §102(b). None of the secondary references are understood to suggest or disclose and are not urged by Paper No. 9 to suggest or disclose the series of steps including the use of a reference sequence which is required by the claims now pending. Further, there is no suggestion of any quantification procedure of the kind defined by claims 31-33.

The pending claims 18-25 are free of the art.

The Objection and Rejection
Under 35 U.S.C. §112, First Paragraph

Paper No. 9 objects to the specification as lacking enablement for the phrase "process for minimizing false negative data". This phrase does not appear in claim 18 as rewritten. The rewritten claims conforms precisely to the specification. The rejection is no longer appropriate.

Previously pending claims 18-25 were rejected under 35 U.S.C. §112, first paragraph "as enabling only for claims limited to the sequences disclosed at pages 4-6 of the specification". The invention, as illustrated by the foregoing table, does not depend on any particular sequence. No undue experimentation would be required to practice the invention as now claimed. More particularly, a person skilled in the art could readily select sequences and from knowledge of the sequences, appropriate primers for use in the claimed invention.

Reconsideration of the rejection of previously pending claims 18-25 under 35 U.S.C. §112, second paragraph as being "indefinite" is requested. It is respectfully suggested that the bases for this rejection have been removed by the amendment of the involved claims which are still pending.

In particular, the phrase "reference sequence" has been provided with a proper antecedent basis. The meaning of reference sequence is now believed to be clear. The "construction of 'synthetic RNA'" and the "length of the 'target'" do not form a part of the invention. Withdrawal of the rejection under 35 U.S.C. §112 based on those expressions is requested.

Claims 19 and 20-25 have been rewritten or amended, thus avoiding the §112 rejections directed to those claims.

Provisional Double Patenting Rejections

Claims 18-30 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 24-53 of co-pending application Serial No. 07/180,740 and claims 10-16 of co-pending application Serial No. 07/355,296.

As regards the rejection based on Serial No. 07/180,740, care will be taken to maintain an appropriate line of demarcation between the claims which may be allowed in that case and claims which may be allowed in this case. If it ultimately seems appropriate to do so, the claims may be consolidated in a single application, depending upon which claims are allowed in the further prosecution of these cases. As regards Serial No. 07/355,296, that application has been abandoned.

As suggested by Paper No. 9, an information disclosure statement is concurrently transmitted.

THE INFORMATION DISCLOSURE STATEMENT

Referring to the references cited in the Information Disclosure Statement, Slamon and Kraus do not describe a co-amplification assay. Chelly, published in June, 1988 is not prior art with respect to this application because the inventions defined by the pending claims were first disclosed at least as early as parent application Serial No. 07/148,959. See, e.g., the Abstract.

With regard to Sninsky, U.S. patent 5,008,182, positive controls are referenced in the paragraph beginning in line 59 of column 15. See also Example I, line 14, column 16 and claims 24 (referring to positive and negative controls) and 26. The Sninsky controls may test for the binding of the primers to the control HIV sequence and an amplification product may be observed when the Sninsky assay is working, but may not be observed when the assay is not working. The controls of Sninsky merely provide for determination of the binding of the primers to the HIV control sequence, but do not monitor false positive and false negative data in the way required by by claim 18 as illustrated by the foregoing table.

Respectfully submitted,

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